

Non-AIDS defining cancer

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Objectives

- Epidemiology of non-AIDS defining cancers (NADC)
- NADC risk factors
- Identify specific NADC that disproportionately affect the HIV+ population
- General diagnosis and treatment of specific NADC
- NADC screening guidelines, if available



RECAP

Which of the following are the AIDS-defining cancers?

- A. Lung cancer, colon cancer, breast cancer
- B. Prostate cancer, non-Hodgkin lymphoma, pancreatic cancer
- C. Myeloblastic leukemia, invasive head and neck cancer, Kaposi sarcoma
- D. Kaposi sarcoma, non-Hodgkin lymphoma, invasive cervical cancer



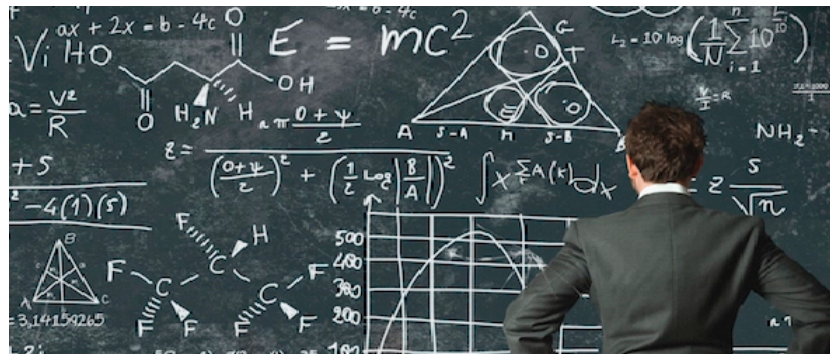
RECAP

- The AIDS-defining cancers (ADC)
 - Kaposi Sarcoma
 - Non-Hodgkin Lymphoma
 - Invasive Cervical Cancer

 - Opportunistic diseases!
 - Highly associated with immunosuppression

Non-AIDS defining cancers

- These include any cancer that isn't ADC, which may (or may not) disproportionately affect HIV+ individuals
- The association with immunosuppression depends on the unique cancer type, and is more complicated.



Non-AIDS defining cancer

- Cancers that disproportionately affect the HIV-infected population
 - Hodgkin lymphoma (HL)
 - Hepatocellular carcinoma
 - Lung cancer
 - Head and neck squamous cell carcinoma
 - Anal cancer

Over the past 2 decades, the incidence
in Non-AIDS defining cancers is:

- A. Increasing
- B. Decreasing
- C. Unchanged

Non-AIDS defining cancer

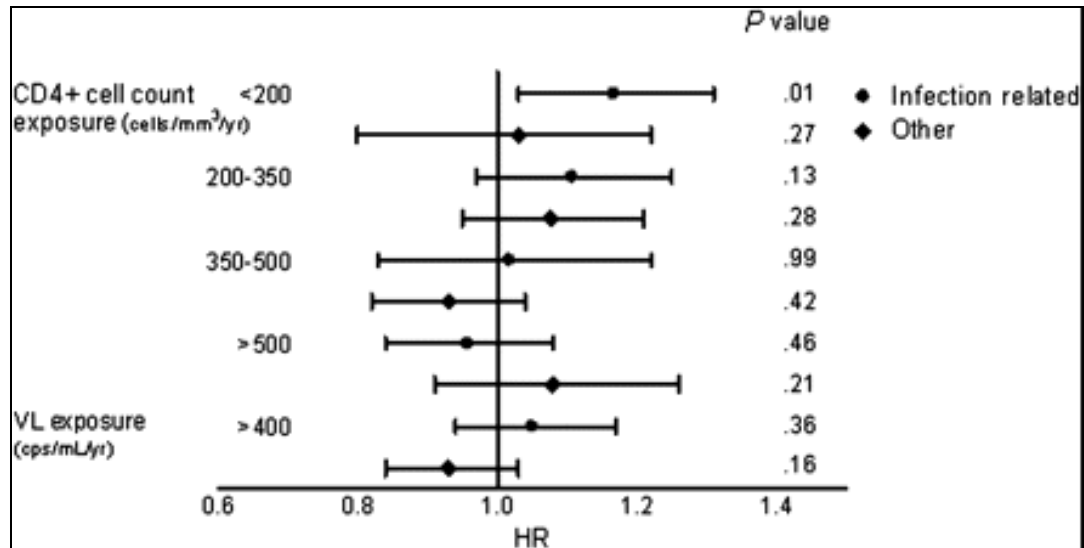
- Increasing incidence in the contemporary ART era
 - 4-fold cancer incidence increase from 1991 – 2005 (96,179 – 413,080 cases)
 - Now the leading cause of death among ART-experienced
 - AIDS-defining cancers decreased during same period

Non-AIDS defining cancer

- Role of immunosuppression
 - Both the HIV-infected population and solid organ transplant population are disproportionately affected by most cancer types
 - Immune deficiency is likely a strong contributor of oncogenesis in HIV overall

Non-AIDS defining cancer

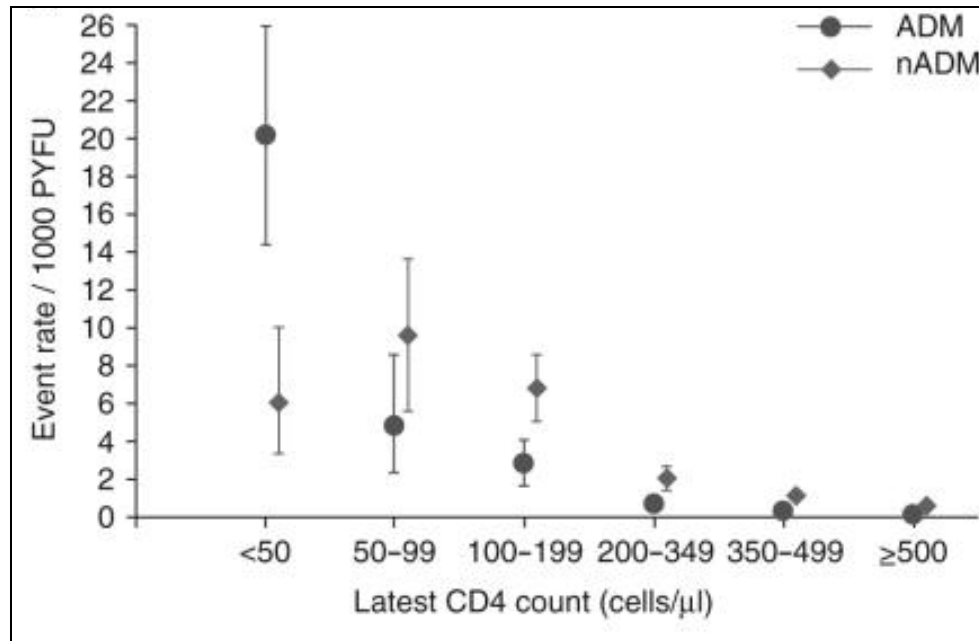
- Duration of CD4 <200 cells/uL associated with higher risk of malignancy



1.12/year [95% CI, 1.03–1.22]

Non-AIDS defining cancer

- Higher risk of malignancy based on depth of recent CD4 count



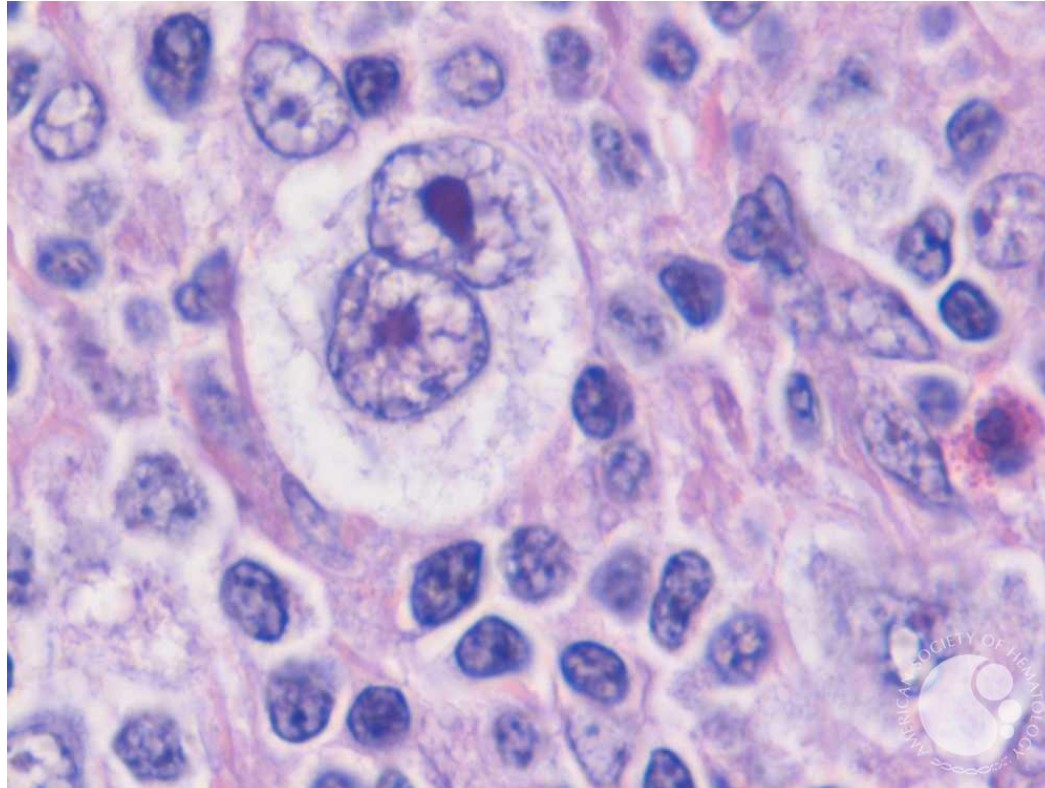
CD4 <50: 6.0 (95% CI 3.3, 10.1)

CD4 >500: 0.6 (95% CI 0.4, 0.8)

Non-AIDS defining cancer

- Other potential contributors:
 - Chronic immune activation/inflammation of HIV infection
 - Aging HIV-infected population
 - Higher smoking and EtOH-abuse prevalence of HIV-infected population
 - Co-infections with other viruses

Hodgkin Lymphoma



Hodgkin Lymphoma

- Risk in HIV infection is 10-25x higher than among general population
- HL tends to have more high-risk characteristics in HIV
- HIV-infected patients have more:
 - B Symptoms
 - Extra-nodal disease
 - Bone marrow involvement



Hodgkin Lymphoma

- High-risk features
 - Mixed cellularity histological subtype
 - Epstein-Barr virus (EBV) infection of the tumor cells
 - Advanced stage
 - Higher International Prognostic Score (IPS)

Hodgkin Lymphoma

- Outcomes are poorer
 - Predictive factors:
 - >45 years of age*
 - Male gender
 - Stage IV disease
 - Low albumin
 - Anemia
 - Lymphopenia
 - Leukocytosis



*Age >45 has been found to be significantly associated with progression or death (RR 8.1)!

Spina M, Carbone A, Gloghini A, et al. Hodgkin's Disease in Patients with HIV Infection. *Adv Hematol* 2011;2011. pii: 402682.

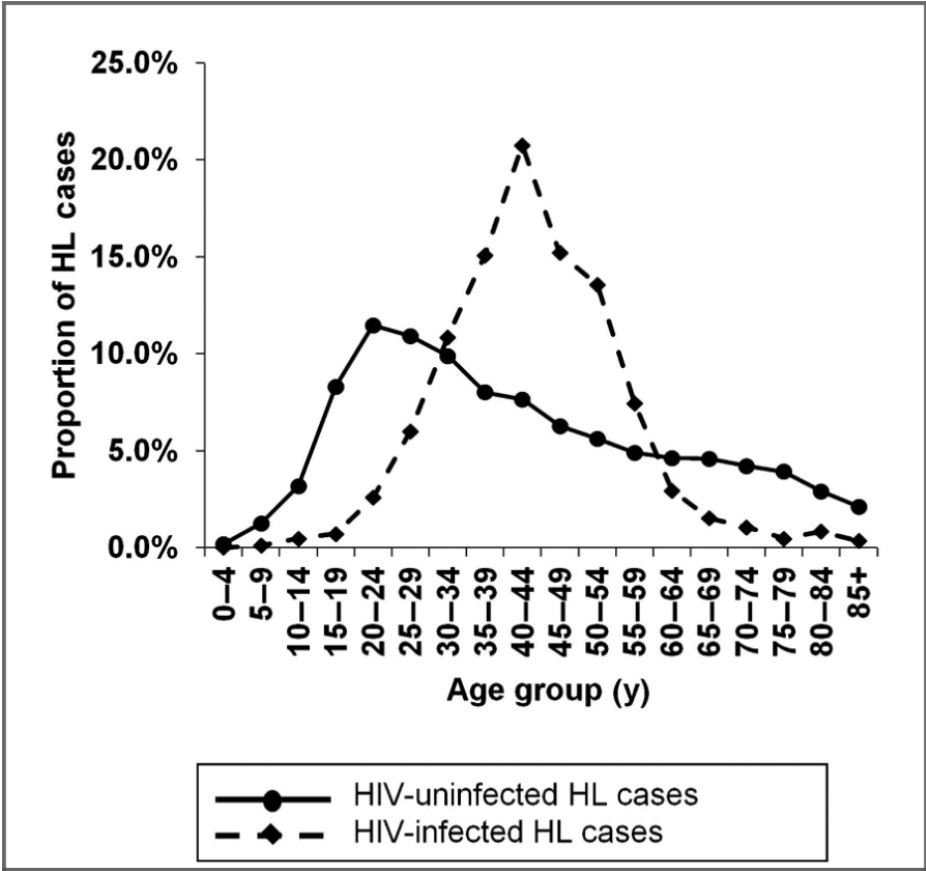
Aries J, Montoto S. Managing HIV and Hodgkin lymphoma in the twenty-first century. *Curr Hematol Malig Rep*. 2014 Sep;9(3):227-32.

Besson C, et al. High Risk Features Contrast With Favorable Outcomes in HIV-associated Hodgkin Lymphoma in the Modern cART Era, ANRS CO16 LYMPHOVIR Cohort. *Clinical Infectious Diseases*, 2015

Which age group is at highest risk for Hodgkin Lymphoma among the HIV+ population?

- A. 20-25
- B. 25-35
- C. 35-45
- D. 45-55
- E. >55

Hodgkin Lymphoma



Hodgkin Lymphoma is most likely to occur at which CD4 count?

- A. <50 cells/ μ L
- B. 50 cells/ μ L
- C. 100 cells/ μ L
- D. 200 cells/ μ L
- E. >200 cells/ μ L

Hodgkin Lymphoma

- Most cases occur at relatively high CD4 counts (>200 cells/ μ L)
 - Fast gain in CD4 T-cells after starting ART is associated with development of HL
 - Possible that CD4 T-cells support development of Reed-Sternberg cells
 - Immune reconstitution may contribute to the development of HL
- 80-100% associated with EBV (higher than in non-HIV HL)



Spina M, Carbone A, Gloghini A, et al. Hodgkin's Disease in Patients with HIV Infection. Adv Hematol 2011;2011. pii: 402682.

Little RF, Dunleavy K. Update on the treatment of HIV-associated hematologic malignancies. Hematol Am Soc Hematol Educ Program. 2013;2013:382-8.

Hodgkin Lymphoma

- HIV-associated HL tends to be unfavorable histological subtypes
 - Nodular sclerosis - 30% (HIV+) vs. 60% (HIV-)
 - Mixed cellularity - 25% (HIV+) vs. 12% (HIV-)
 - Lymphocyte deplete – 4% (HIV+) vs. 1% (HIV-)

**HIGH
RISK**

Hodgkin Lymphoma

- Treatment
 - ABVD is standard therapy
 - ART can and should be used concurrently
 - Avoid PIs due to CYP450 3A4 interactions
 - Ritonavir can exacerbate vinblastine-induced neurotoxicity and neutropenia
 - Despite higher prevalence of high-risk features in HIV infection, prognosis is now on par with that of the general population.
 - ART is crucial

Hepatocellular carcinoma



Hepatocellular carcinoma

- Usually secondary to HBV or HCV co-infection
- Process is accelerated by HIV (increases HCC risk 7-fold)
 - Time to develop HCC after HCV infection is about 10 years shorter in setting of HIV
 - HIV increases risk of development of chronic HCV
 - HIV increases rate of fibrosis

Hepatocellular carcinoma

- Incidence varies by country
 - Highest in HBV endemic countries of East Asia, Africa
 - In developed countries, most are in HIV/HCV co-infection
 - Up to 25% of HIV+ patients have chronic HCV
 - 5-10% of HIV+ patients have chronic HBV

Hepatocellular carcinoma

- Usually asymptomatic initially
- Clinical presentation varies significantly depending on tumor growth rate, burden, number and location

Hepatocellular carcinoma

- HCC in HIV infection:
 - More advanced/infiltrative at diagnosis
 - More advanced cirrhosis at diagnosis
 - Younger age at diagnosis
 - Higher alpha-fetoprotein levels
 - Worse survival
 - Though not significantly worse if early stage

Hepatocellular carcinoma

- Curative treatment
 - Surgical resection
 - Radiofrequency ablation
 - Ethanol injection
 - Orthotopic liver transplantation
- Palliative treatment
 - Transarterial chemoembolization (TACE)
 - Kinase inhibitors
 - Sorafenib
 - Sunitinib
 - Erlotinib
 - Systemic chemotherapy

Hepatocellular carcinoma

- Primary prevention
 - HBV vaccination
 - HCV screening and treatment
 - IVDU counseling
 - EtOH avoidance
 - Screening in cirrhotic patients



Lung cancer



Lung cancer

- Higher incidence among HIV+ adults (about 2-fold) than HIV- adults in USA
- Significant associations include older age, smoking >10 years, h/o Pneumocystis or recurrent pneumonia, h/o asthma

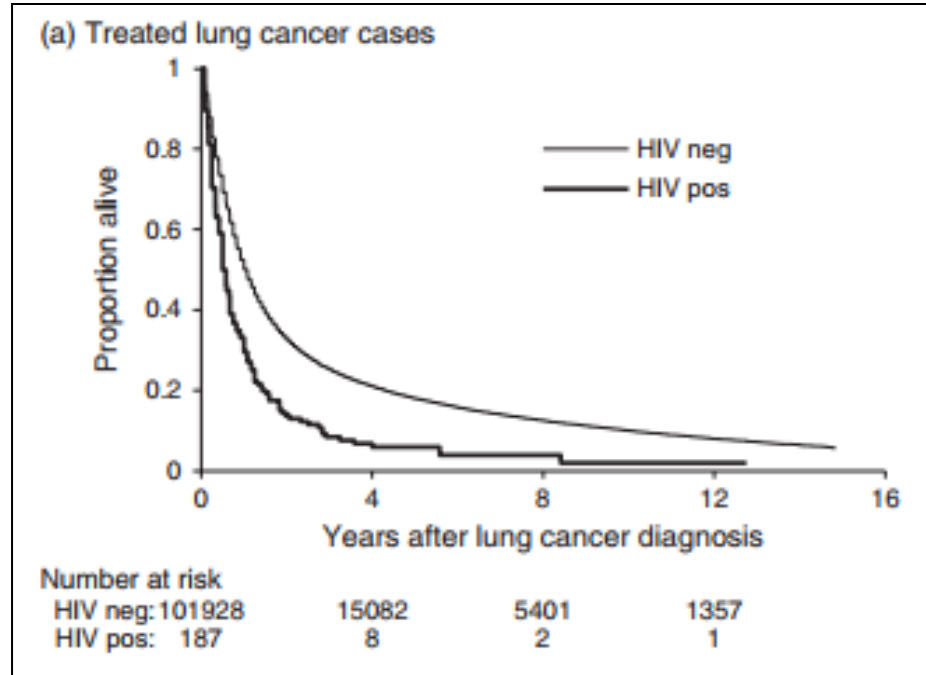


Lung cancer

- HIV+ with lung cancer
 - Tend to be younger
 - Present with more advanced disease
 - Have worse overall survival
 - May receive treatment less frequently
 - HIV+ adults found to be less likely to receive potentially curative resection
 - Less likely to receive chemotherapy, radiation

Lung cancer

- Survival



Head and Neck Squamous Cell Carcinoma



Head and Neck Squamous Cell Carcinoma

- Higher incidence of head and neck cancer (2 – 4-fold) in HIV infection
- HIV+ population has a higher prevalence of primary risk factors
 - Tobacco use
 - EtOH use
 - Oral HPV infection (2-fold higher)
 - More sexual partners

Head and Neck Squamous Cell Carcinoma

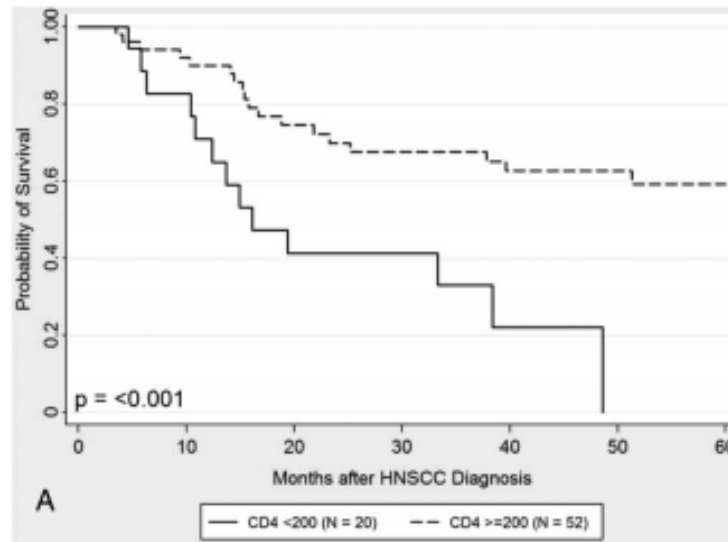
- 2 – 4-fold higher in HIV infection than among general population
 - Much more modest increased risk in HIV infection than among other HPV-associated cancers
 - Extent of HPV association in HIV infection is not well-characterized
 - Other factors are likely contributing
 - Immunosuppression
 - Tobacco use

Head and Neck Squamous Cell Carcinoma

- HIV+ adults with head and neck cancer:
 - Are mostly men, 91% (vs 68% among HIV-)
 - Are younger, median age 50 years (vs 62 years)
 - Are mostly nonwhite, 49% (vs 18%)
 - Are mostly current smokers, 61% (vs 18%)
 - Present at advanced stage, 60% (vs 20%)

Head and Neck Squamous Cell Carcinoma

- Poor survival outcome associations:
 - Current smoking (in both HIV+ and HIV-)
 - Lower CD4 count at diagnosis
 - Poor prognosis associated with immunosuppression



Anal Cancer

- HPV-associated
- Incidence has not decreased in the contemporary ART era, likely increasing
- Highest risk population: HIV+ MSM, risk up to 128/100,000 (vs ~1.5-2/100,000 in the general population)
- The quadrivalent HPV vaccine has been shown to reduce anal HPV infection and neoplasia in men

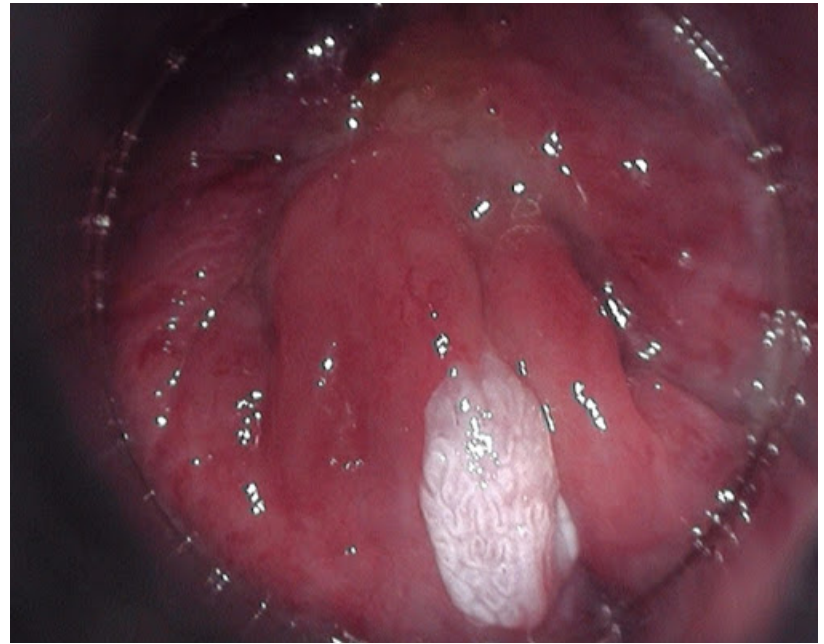
Anal Cancer

- There are no national recommendations for routine anal cancer screening, but should be strongly considered in HIV-infected MSM and women (especially if history of other HPV-related lesions)
- Anal cancer screening should NOT be performed without the availability of high-resolution anoscopy (HRA)

Anal cancer

- Appropriate screening would include both cytology, HPV cotesting and DRE
- Abnormal cytology (ASCUS and LSIL), should get high-resolution anoscopy
- Any palpable masses on DRE or HSIL – referral to colorectal surgery
- Consider annual screening after normal cytology

High Resolution Anoscopy



Pahissa A, Villar S

Conclusions

- HIV-infected adults are at disproportionately high risk of many cancer types
- Contributing factors include immunosuppression, chronic inflammation, co-infections, and behaviors/exposures
- Outcomes are generally worse for HIV-infected patients
- Cancer prevention is a cornerstone of HIV care
 - Especially among those at high risk (i.e. chronic HCV)

Thank you!